

WE CLAIM:

1. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:
 - (a) one or more target binding domains that target binding of the nucleic acid molecule to a target pre-mRNA expressed within the cell;
 - (b) a 3' splice region comprising a 3' splice acceptor site;
 - (c) a spacer region that separates the 3' splice region from the target binding domain; and
 - (d) a nucleotide sequence encoding a light producing protein or enzyme to be *trans*-spliced to the target pre-mRNA;wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.
2. The cell of claim 1 wherein the 3' splice region further comprises a branch point and a pyrimidine tract.
3. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:
 - (a) one or more target binding domains that target binding of the nucleic acid molecule to a target pre-mRNA expressed within the cell;
 - (b) a 5' splice site;

- (c) a spacer region that separates the 5' splice site from the target binding domain; and
- (d) a nucleotide sequence encoding a light producing protein or enzyme to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

4. The cell of Claim 1 or 2 wherein the nucleic acid molecule further comprises a 5' donor site.

5. A method of producing a chimeric mRNA molecule in a cell wherein said chimeric molecule expresses a light producing protein or enzyme comprising contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- (a) one or more target binding domains that target binding of the nucleic acid molecule to a target pre-mRNA expressed within the cell;
- (b) a 3' splice region comprising a 3' splice acceptor site;
- (c) a spacer region that separates the 3' splice region from the target binding domain; and
- (d) a nucleotide sequence encoding a light producing protein or enzyme to be *trans*-spliced to the target pre-mRNA;

under conditions in which a portion of the nucleic acid molecule is *trans*-spliced to a portion of the target pre-mRNA to form a chimeric mRNA within the cell.

6. The method of claim 5 wherein said 3' splice region further comprises a branch point and a pyrimidine tract.

7. A method of producing a chimeric mRNA molecule in a cell wherein said chimeric molecule expresses a light producing protein or enzyme comprising contacting a target pre-mRNA expressed within the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- (a) one or more target binding domains that target binding of the nucleic acid molecule to a target pre-mRNA expressed within the cell;
- (b) a 5' splice site;
- (c) a spacer region that separates the 5' splice site from the target binding domain; and
- (d) a nucleotide sequence encoding a light producing protein or enzyme to be *trans*-spliced to the target pre-mRNA;

under conditions in which a portion of the nucleic acid molecule is *trans*-spliced to a portion of the target pre-mRNA to form a chimeric mRNA within the cell.

8. The method of Claim 5 or 6 wherein the nucleic acid molecule further comprises a 5' donor site.

9. A nucleic acid molecule comprising:

- (a) one or more target binding domains that target binding of the nucleic acid molecule to a target pre-mRNA expressed within a cell;
- (b) a 3' splice region comprising a 3' splice acceptor site;
- (c) a spacer region that separates the 3' splice acceptor site from the target binding domain; and
- (d) a nucleotide sequence encoding a light producing protein or enzyme to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

10. The nucleic acid molecule of claim 9 wherein the 3' splice region further comprises a branch point and a pyrimidine tract.

11. A nucleic acid molecule comprising :

- (a) one or more target binding domains that target binding of the nucleic acid molecule to a target pre-mRNA expressed within a cell;
- (b) a 5' splice site;
- (c) a spacer region that separates the 5' splice site from the target binding domain; and

- (d) a nucleotide sequence encoding a light producing protein or enzyme to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

12. The nucleic acid molecule of claim 9 or 10 wherein the nucleic acid molecule further comprises a 5' donor site.

13. A method for targeting cell death comprising:

(i) contacting said cell with a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a target pre-mRNA expressed within the cell;
- b) a 3' region comprising a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence encoding a light producing protein enzyme to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell; and

(ii) placing a photosensitizer in close enough proximity to the cell to permit activation of the photosensitizer by the light producing enzyme, wherein said activation results in cell death.

14. The method of claim 13 wherein said 3' splice region further comprises a branch point and a pyrimidine tract.

15. A method for targeting cell death comprising:

(i) contacting said cell with a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a target pre-mRNA expressed within the cell;
- b) a 5' splice site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence encoding a light producing protein enzyme to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell; and

(ii) placing a photosensitizer in close enough proximity to the cell to permit activation of the photosensitizer by the light producing enzyme, wherein said activation results in cell death.

16. The method of claim 13 or 14 wherein the nucleic acid molecule further comprises a 5' donor site.

17. The method of claim 13, 14 or 15 further comprising contacting said cell with a substrate specific for the light producing protein or enzyme.

18. The method of claim 16 further comprising contacting said cell with a substrate specific for the light producing protein or enzyme.

19. A recombinant conditionally replicative adenovirus comprising a transgene wherein said transgene encodes one or more pre-*trans*-splicing molecules wherein said pre-*trans*-splicing molecules comprise :

- a) one or more target binding domains that target binding of the pre-*trans*-splicing molecule to a target pre-mRNA expressed within a cell;
- b) a 3' splice region comprising a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a polypeptide selected from the group consisting of (i) an adenovirus polypeptide; or (ii) a polypeptide that functions as a light inducing enzyme or protein.

20. The recombinant conditionally replicative adenovirus of claim 19 wherein said 3' splice region further comprises a branch point and a polypyrimidine tract.

21. A recombinant conditionally replicative adenovirus comprising a transgene wherein said transgene encodes one or pre-*trans*-splicing molecules wherein said pre-*trans*-splicing molecules comprise :

- a) one or more target binding domains that target binding of the pre-*trans*-splicing molecule to a target pre-mRNA expressed within a cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a polypeptide selected from the group consisting of (i) an adenovirus polypeptide; or (ii) a polypeptide that functions as a light inducing enzyme or protein.

22. The adenovirus of claim 20 or 21 wherein the pre-*trans*-splicing molecule further comprises a 5' donor site.

23. A recombinant conditionally replicative adenovirus comprising

- (i) a transgene wherein said transgene encodes a pre-*trans*-splicing molecules wherein said pre-*trans*-splicing molecules comprises :
 - a) one or more target binding domains that target binding of the pre-*trans*-splicing molecule to a target pre-mRNA expressed within a cell;
 - b) a 3' splice region comprising a 3' splice acceptor site;

- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes an adenovirus polypeptide; and

(ii) a transgene encoding a light producing protein or enzyme.

24. The recombinant conditionally replicative adenovirus of claim 23 wherein said 3' splice region further comprises a branch point and a polypyrimidine tract.

25. A recombinant conditionally replicative adenovirus comprising

(i) a transgene wherein said transgene encodes a pre-*trans*-splicing molecule wherein said pre-*trans*-splicing molecule comprises :

- a) one or more target binding domains that target binding of the pre-*trans*-splicing molecule to a target pre-mRNA expressed within a cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and

- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes an adenovirus polypeptide; and
- (ii) a transgene encoding a light producing enzyme or protein.

26. The adenovirus of claim 23 or 24 wherein the pre-*trans*-splicing molecule further comprises a 5' donor site.

27. A method for targeting cell death comprising contacting said cell with the conditionally replicative adenovirus capable of encoding a light producing enzyme or protein.